



RESPONSE TO COMMENT ON HEDDERSON ET AL.

Prepregnancy SHBG Concentrations and Risk for Subsequently Developing Gestational Diabetes Mellitus. *Diabetes Care* 2014;37:1296–1303

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We appreciate the comment by Stefan et al. (1) on our recent article (2). We agree that HOMA-IR is not the ideal method to assess insulin resistance and a more dynamic test, e.g., a frequently sampled 75-g oral glucose tolerance test, would have been more precise. Without this more accurate assessment, it is difficult to know for certain whether our observed association between sex hormone-binding globulin (SHBG) and odds of gestational diabetes mellitus (GDM) is entirely independent of insulin resistance. Unfortunately, those data were not available and are often not practical for large epidemiologic studies. We also agree that SHBG may be a marker of liver fat content. Upon reading this comment, we ran a multiple adjusted re-

gression model of SHBG and GDM that additionally adjusted for the liver enzyme γ -glutamyl transferase and HOMA-IR and found that the association between being in the lowest two quartiles of SHBG compared with being in the highest quartile of SHBG GDM risk remained significant (odds ratio 4.34, 95% CI 2.15–9.78 and 2.48, 95% CI 1.25–4.94, respectively). So to the extent that γ -glutamyl transferase is a marker of liver fat accumulation, our observation suggests that perhaps SHBG may also have an independent effect. However, the concern raised by Stefan et al. (1) highlights the need for future studies with better measures of insulin resistance and liver fat accumulation to clarify the potential mechanism behind our observation. Nevertheless, we agree

with the conclusion of Stefan et al. that our article does add to the literature suggesting that hepatokines play an important role in glucose metabolism.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Stefan N, Peter A, Häring H-U. Comment on Hedderson et al. Prepregnancy SHBG concentrations and risk for subsequently developing gestational diabetes mellitus. *Diabetes Care* 2014;37:1296–1303 (Letter). *Diabetes Care* 2014;37:e278–e279. DOI: 10.2337/dc14-1272
2. Hedderson MM, Xu F, Darbinian JA, et al. Prepregnancy SHBG concentrations and risk for subsequently developing gestational diabetes mellitus. *Diabetes Care* 2014;37:1296–1303

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